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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,627	08/19/2003	Johan Sundelin	MPI93-006CP1DV1ACN1DV1M	4455

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EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,627	SUNDELIN ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-28, 44-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *46,47,57 and 58* is/are allowed.

6)☒ Claim(s) *27,28,44,45,48,50-56 and 59-69* is/are rejected.

7)☒ Claim(s) *49* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The indicated allowability of claims 53-56 is withdrawn in view of the newly applied rejections under 35 USC 112, 1st paragraph.

35 USC 103(a) Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27, 59, 63, 64 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coughlin in view of Carney et al.

Applicants claim an isolated polypeptide having at least 15 consecutive amino acids encoded by a nucleic acid molecule that hybridizes under stringent conditions to a nucleic acid molecule complementary to SEQ ID NO:3 or 62 wherein the polypeptide

has a biological activity in common with C140. Applicants also claim a polypeptide comprising a 10 consecutive amino acid sequence of SEQ ID NO:4 or 63. It is noted that the sequence of human thrombin receptor (as taught by Coughlin, see below) contains a 10 consecutive amino acid stretch (LNITTCHDVL) in common with the C140 receptor polypeptide and, like the C140 receptor, the human thrombin receptor is apparently a protease activated receptor (biological activity in common). With regard to claims 27 and 59, it is noted that the nucleic acid encoding the LNITTCHDVL sequence and flanking sequences are sufficient to encode a 15 consecutive amino acid sequence that is approximately 80% homologous to the corresponding nucleotide sequences of SEQ ID NO:3 or 62. It must be assumed, absent evidence to the contrary, that the sequence encoding the thrombin polypeptides would be capable of hybridizing, under the stringency conditions recited in the claims, to the nucleic acids complementary to SEQ ID NO: 3 or 62.

Coughlin (US 5,256,766, issued 10/26/93, filed 2/19/91, see whole document, particularly Fig. 1A-1B, columns 2-3) recites the human thrombin receptor DNA and protein sequence. Coughlin recites the isolation, cloning and expression of the human thrombin gene as well as making antibodies to the human thrombin protein. Coughlin however, does not specifically prepare the human thrombin polypeptide in isolated form.

Carney et al. (US 5,352,664, issued 10/4/94, filed 10/31/86, see whole document, particularly column 14) recites that affinity purification of the thrombin receptor can be accomplished.

The ordinary skilled artisan, seeking to generate an isolated polypeptide with the claimed characteristics (i.e. human thrombin receptor) would have been motivated to express the protein as recited by Coughlin and subsequently isolate the protein by a procedure such as affinity purification because isolation of the protein would be necessary in order to generate antibodies specific to the protein. It would have been obvious for the ordinary skilled artisan to do this because a purified isolated protein is necessary in order to generate antibodies which are specific to the protein. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

35 USC 112, 1st Paragraph Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27, 28, 44, 45, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated polypeptides consisting of SEQ ID NO:4 and 63 or polypeptides having at least 15 consecutive amino acids of SEQ ID NO:4 or 63, does not reasonably provide enablement for any isolated polypeptide having at least 15 consecutive amino acids and being encoded by a nucleotide sequence capable of hybridizing under stringent conditions to the

complements of SEQ ID NO:3 or 62 or to any polypeptide having at least 75% or 90% or 95% amino acid sequence identity to either SEQ ID NO:4 or 63. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants claim polypeptides, without any recited function, which have certain amino acid sequence identities to SEQ ID NO:4 or 63 or amino acid sequences having at least 15 consecutive amino acids and are encoded by a nucleic acid capable of hybridizing to the complement of SEQ ID NO:3 or 62. Applicants have not taught how to the use amino acid sequences which are not C140 polypeptides or portions of C140 proteins.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

1) Unpredictability of the art. The art with regard to use of polypeptides with no known function must be considered unpredictable. If the function of the polypeptide is

unknown, its use for any reasons in any experiment would be unpredictable because its' functional characteristics are unknown.

2) State of the art. The state of the art with regard to making and using polypeptides, with no recited function, which share at least 75% or 90% or 95% amino acid sequence identity with SEQ ID NO:4 or 63 or have at least 15 consecutive amino acids and are encoded by a nucleic acid capable of hybridizing to the complement of SEQ ID NO:3 or 62 is nil.

3) Number of working examples. Applicants present no working examples of the claimed invention.

4) Amount of guidance provided. Applicants provide no guidance on making and using the claimed polypeptides with no recited function.

5) Scope of the invention. The scope of the invention must be considered broad and reads on millions of different polypeptides with no recited function.

6) Nature of the invention. The invention involves the making and use of polypeptides with no recited function.

7) Level of skill in the art. The level of skill in the art must be considered to be high; however, given the unpredictability of the art, the lack of guidance by the applicants, the lack of any working examples and the broad scope of the claims, it must be considered that the skilled artisan would have had to have conducted trial and error experimentation in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in ascertaining whether a claimed invention is enabled, it must be considered

that the skilled artisan would have had to have conducted undue and excessive experimentation in order to practice the claimed invention.

Claims 27, 28, 44, 45, 50, 51, 53-56, 66 and 67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim any isolated polypeptides, **with no recited functions**, having least 15 consecutive amino acids and being encoded by a nucleotide sequence capable of hybridizing under specifically claimed stringent conditions to the complements of SEQ ID NO:3 or 62 or to any polypeptide (with no recited functions) having at least 75% or 90% or 95% amino acid sequence identity to either SEQ ID NO:4 or 63. The application as originally filed, provides support for isolated C140 polypeptides having at least 15 consecutive amino acid residues and for C140 polypeptides having at least 75% or 90% or 95% amino acid sequence identity to a "common C140 receptor sequence" (i.e. either SEQ ID NO:4 or 63. The application, as originally filed, does not provide support for **any isolated polypeptides, with no recited functions**, having least 15 consecutive amino acids and being encoded by a nucleotide sequence capable of hybridizing under specifically claimed stringent conditions to the complements of SEQ ID NO:3 or 62 or to any polypeptide (**with no recited functions**) having at least 75% or 90% or 95% amino

acid sequence identity to either SEQ ID NO:4 or 63. No support for the limitation of a polypeptide having at least 15 consecutive amino acids and encoded by a nucleic acid capable of hybridizing, under the claimed stringent hybridization conditions, to the complements of SEQ ID NO:3 or 62 can be found.

With regard to the limitations of claims 53-56, 66 and 67, the application as originally filed, does not provide support for the claimed polypeptide fragments encoded by the **specific nucleotides** claimed (56-1249 of SEQ ID NO:3 or 50-1240 of SEQ ID NO:62) or the specific isolated polypeptide fragments claimed (an isolated fragment comprising amino acids 1-37 or 31-37 of SEQ ID NO:4 or amino acids 1-36 or 30-36 of SEQ ID NO:63). It is noted that applicants, in a preliminary amendment filed with the transmittal papers (8/19/03) of the instant application added the limitations recited in claims 53-56, 66 and 67. However, since the instant application was filed prior to 09/21/2004 and the amendment was not referred to in the **first executed oath or declaration**, the preliminary amendment is not considered part of the original disclosure and the added limitations hence represent impermissible new matter. This is a NEW MATTER rejection.

Claims 52 and 59-69 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim an isolated polypeptide having at least 15 consecutive amino acids encoded by a nucleic acid capable of hybridizing, under the claimed stringent hybridization conditions, to the complements of SEQ ID NO:3 or 62 and wherein said polypeptide has a biological activity (C140 receptor function or effector function or cross-reactive antigenicity or comprises an activated C140 receptor) in common with C140. Applicants also claim an isolated polypeptide comprising a portion (at least 10 consecutive amino acids) of SEQ ID NO:4 or 63 or specific portions of SEQ ID NO:63.

Applicants disclose the human C140 cDNA and genomic sequences (SEQ ID NO:3, 62) and the polypeptide sequences of human C140 (SEQ ID NO:4, 63), peptide agonists and antagonists of human C140 wherein said agonists and antagonists are C140 peptides as well as murine C140 DNA and polypeptide sequences. The instant claims read on a genus of isolated polypeptide sequences encoding an activated C140 receptor or a genus of polypeptides having a biological activity (C140 receptor function or effector function or cross-reactive antigenicity or comprises an activated C140 receptor) in common with C140. The claims also read on a genus of polypeptides comprising portions of SEQ ID NO:4 or 63 and hence the polypeptides can read on fusion proteins with the recited portions of the SEQ ID NO:4 or 63 or other C140 molecules comprising the recited portions of SEQ ID NO:4 or 63. Applicants define the scope of polypeptides encompassed within the definition of "C140 receptor polypeptides" on page 13 of the specification as follows:

C140 receptor polypeptides include those containing predetermined mutations by, e.g., homologous recombination, site-directed or PCR mutagenesis, and CI40 receptor polypeptides of other animal species, including but not limited to rabbit, rat, murine, porcine, bovine, ovine, equine and non-human primate species, and alleles or

other naturally occurring variants of the C140 receptor of the foregoing species and of human sequences; derivatives of the commonly known C140 receptor or its fragments wherein the C140 receptor or its fragments have been covalently modified by substitution, chemical, enzymatic, or other appropriate means with a moiety other than a naturally occurring amino acid (for example a detectable moiety such as an enzyme or radioisotope); glycosylation variants of Cl40 receptor (insertion of a glycosylation site or deletion of any glycosylation site by deletion, insertion or substitution of appropriate amino acid); and soluble forms of C140.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention (See MPEP 2163). In the present case, applicants have not presented a correlation between the structure of the claimed C140 receptor molecules and the function of those molecules as C140 receptors. For example, applicants claim C140 receptor polypeptides from other animal species and with the exception of mice, applicants have not disclosed the structure of any other C140 receptor polypeptides. Applicants have disclosed no variants of the human or mouse C140 receptor polypeptides. While applicants have characterized the human (and murine) C140 receptor molecule with regard to it's being a member of the large and diverse G protein coupled receptor family (i.e. having seven transmembrane regions common to said proteins) as well as having **potential** asparagine linked glycosylation sites and a **putative** protease receptor cleavage site at Arg34-Ser35, applicants have not disclosed

the regions of the molecule which would be conserved and are essential for activity. It is noted that the art is replete with examples of numerous other G protein coupled receptors which have seven transmembrane regions and putative protease cleavage sites (See for example, Shi et al., Mol. Cancer Res., 2004, Vol. 2(7), pp. 395-402). Without elucidation of the sequences which are essential for a protein to be recognized as a C140 receptor polypeptide, the skilled artisan would not be able to recognize whether any given polypeptide containing a putative protease receptor cleavage site and seven transmembrane regions characteristic of hundreds of different G protein coupled receptors and protease activated receptors would or would not be a C140 receptor specific polypeptide. Interestingly, in a post filing paper by Blackhart et al. (J. Biol. Chem., 1996, Vol. 271, No. 28, pp. 16466-16471, two of the authors of the paper are the inventors of the instant invention) which deals with ligand cross-reactivity within the known members of the protease activated receptor family, the C140 receptor is not mentioned. Additionally, Blackhart et al. notes that the members of the protease activated receptor family appear to differ widely with regard to function and activation or inhibition by agonist and antagonist peptides, respectively. It must be considered, absent evidence to the contrary, that the two C140 sequences disclosed by applicants are not a representative number of species sufficient to provide a description of the claimed genus. The skilled artisan would therefore not conclude that applicants were in possession of the claimed genus.

Applicants' traverse of the outstanding written description rejection is moot given applicants' amendments to the claims. To the extent that the rejection still applies to

claim 52, it will be briefly addressed. First, it is noted that applicants' arguments are essentially the same as previously presented and addressed by the examiner (See Final rejection, mailed 1/11/06). Applicants assert that the examiner has cited no case law or other authority in support of his position. In response, the examiner directs applicants' attention to MPEP 2163 which provides the rationale and legal framework for rejections under 35 USC 112, 1st paragraph (written description). The examiner has followed the guidelines set forth in the MPEP.

Applicants argue that they have described the human and murine C140 molecules to the extent that the skilled artisan would be able to identify any protein that would fall within the limitations of the claims.

In response, the examiner notes that it is unclear what characteristics of the C140 molecules distinguish them from other protease-activated receptors. The characteristics applicants disclose are common to G-protein-coupled receptors (encompassing hundreds of different receptors with widely varying functions) and are not unique to C140 receptors. Applicants also disclose some putative signal sequences or cleavage sites or activation domains but whether these motifs are diagnostic for C140 proteins or are common to other protease-activated receptors is not disclosed. Finally, the examiner has been unable to uncover any post filing art concerning C140 receptors which adds any further information to that disclosed by applicants.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 48 is vague in the recitation of the phrase "...comprises the amino acid sequences (emphasis added) of SEQ ID NO:63.". Since SEQ ID NO:63 is a single amino acid sequence, it is unclear what additional "sequences" applicants are referring to.

Any rejections not repeated in this Office Action are withdrawn.

Claims 45-47 and 57-58 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DAVID GUZO
PRIMARY EXAMINER

David Guzo
May 22, 2006